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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A KIT FOR MEASURING THE THROMBIN GENERATION IN A SAMPLE OF A PATIENT'S BLOOD OR PLASMA

(57) Abstract: The invention provides a kit for measuring the thrombin generation in a sample of a patient's blood or plasma, or in a sample of clotting factors. The kit contains lyophilized tissue factor/phospholipid-complex and a lyophilized mixture containing a thrombin-substrate and CaCl_2 . The invention also provides processes for preparing the reagents for the kit. The kit can be used in a method for measuring the thrombin generation in a sample, wherein it is possible to detect changes in thrombin generation kinetics, for example after administration of inhibitor bypassing agents to a patient who has developed inhibitors to an exogenous clotting factor such as Factor VIII.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/003328

A. CLASSIFICATION OF SUBJECT MATTER

C12Q1/56 G01N33/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>US 5 418 141 A (ZWEIG ET AL) 23 May 1995 (1995-05-23) column 1, lines 7-59 column 2, lines 30-47 column 3, line 62 - column 4, line 6 column 4, lines 6-45 column 7, lines 6-26 column 9, line 9 - column 11, line 15 column 12, lines 53-58 claims 1,2,4,7</p> <p style="text-align: center;">----- -/--</p>	<p>1-13, 19-23</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

25 August 2005

Date of mailing of the international search report

03. 01. 2006

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98/48283 A (INSTRUMENTATION LABORATORY S.P.A) 29 October 1998 (1998-10-29) page 1, lines 1-6 page 3 - page 4 page 5, lines 1-23 page 10 page 15, lines 1-19 claims 1-8,17-23 -----	1-13, 19-23
A	US 5 314 695 A (BROWN ET AL) 24 May 1994 (1994-05-24) abstract; claims 1,5-7; examples 4-7 -----	1-13, 19-23
A	WO 93/07492 A (BAXTER DIAGNOSTICS INC) 15 April 1993 (1993-04-15) abstract; claims 1-7; figures 1,2; examples 2,4,5 -----	1-13, 19-23
A	US 5 059 525 A (BARTL ET AL) 22 October 1991 (1991-10-22) column 1, line 39 - column 2, line 4 column 2, lines 28-44 -----	1-13, 19-23
A	TURECEK P L ET AL: "Factor VIII inhibitor-bypassing agents act by inducing thrombin generation and can be monitored by a thrombin generation assay." PATHOPHYSIOLOGY OF HAEMOSTASIS AND THROMBOSIS, vol. 33, no. 1, June 2003 (2003-06), pages 16-22, XP002342160 ISSN: 1424-8832 cited in the application the whole document -----	1-13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2005/003328

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-13, 19-23

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-13,19-23

measurement of the thrombin generation in a sample using lyophilized TF/PL-complex and lyophilized mixture containing thrombin-substrate and CaCl_2 .

2. claims: 14-18

process for preparing a lyophilized TF/PL-complex

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2005/003328

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